2-18 3-21 7-22 8-23 11-20 15-24
ring bonds :
1-2 1-6 1-13 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 10-11 11-12 12-13
14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
1-13 2-18 5-7 6-10 7-8 7-22 8-9 9-10 10-11 11-12 12-13 14-15 14-19
15-16 16-17 17-18 18-19
exact bonds :
3-21 8-23 11-20 15-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 14 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS

Stereo Bonds:

20-11 (Single Wedge).

Stereo Chiral Centers:

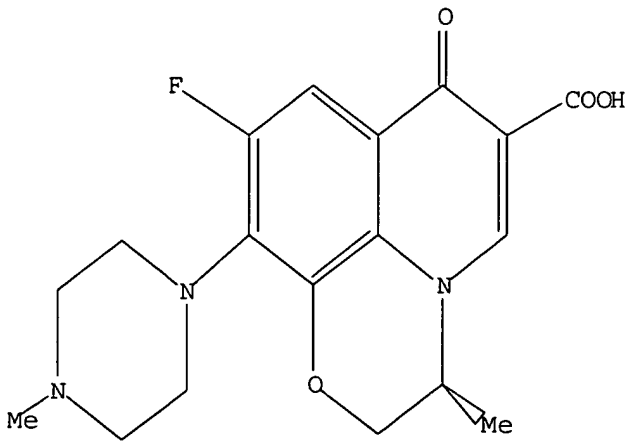
11 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 11

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 12:58:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     27 TO ITERATE

100.0% PROCESSED      27 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          229 TO      851
PROJECTED ANSWERS:               1 TO       80

L2             1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:58:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    500 TO ITERATE

100.0% PROCESSED     500 ITERATIONS                               29 ANSWERS
SEARCH TIME: 00.00.01

L3            29 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               161.33     161.54

FILE 'CAPLUS' ENTERED AT 12:58:40 ON 25 FEB 2005
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FILE COVERS 1907 - 25 Feb 2005  VOL 142 ISS 10
FILE LAST UPDATED: 24 Feb 2005  (20050224/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4         2223 L3

=> s l3 or levofloxacin?
L5         2458 L3 OR LEVOFLOXACIN?

=> s l5 and (crystalline? or anhydrous?)
```

own work

L6 8 L5 AND (CRYSTALLINE? OR ANHYDROUS?)

=> d ibib abs hitstr tot

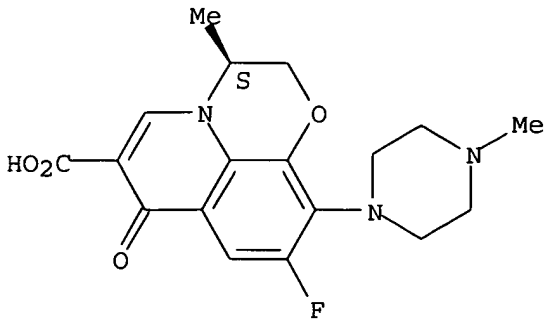
L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:633285 CAPLUS
DOCUMENT NUMBER: 141:162476
TITLE: Novel **anhydrous crystalline** form of **Levofloxacin** and process for its preparation
INVENTOR(S): Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Reddy, Koppera Ravinder; Reddy, Maram Reddy Sahadeva; Prakash, Pitta Jaya
PATENT ASSIGNEE(S): Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004152701	A1	20040805	US 2003-716207	20031118
PRIORITY APPLN. INFO.:			IN 2002-MA898 A	20021202

AB A process for the preparation of an **anhydrous crystalline** form of an antimicrobial agent **Levofloxacin** comprises the condensation of N-methyl-piperazine with S(-)-9,10-difluoro-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-[1,4]-benzoxazine-6-carboxylic acid in acetonitrile followed by distillation of solvent to afford the residue, the resultant residue is refluxed with toluene and the solid is filtered at room temperature to afford the **Levofloxacin.** **Levofloxacin** was further refluxed in acetonitrile, filtered and dried to constant weight to give the **anhydrous crystalline** form of **Levofloxacin.** The **anhydrous crystalline** form of **Levofloxacin** is characterized by X-ray diffractogram, Differential Scanning Calorimetry thermogram and IR Spectra. 1.

IT **100986-85-4P, Levofloxacin**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **anhydrous crystalline** form of **levofloxacin**)
RN 100986-85-4 CAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:754995 CAPLUS
DOCUMENT NUMBER: 137:268473
TITLE: Porous drug matrices and methods of manufacture thereof
INVENTOR(S): Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002142050	A1	20021003	US 2002-53929		20020122
US 6395300	B1	20020528	US 1999-433486		19991104
US 6645528	B1	20031111	US 2000-694407		20001023
ZA 2001010347	A	20030730	ZA 2001-10347		20011218
PRIORITY APPLN. INFO.:			US 1999-136323P	P	19990527
			US 1999-158659P	P	19991008
			US 1999-433486	A2	19991104

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in **crystalline** form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has

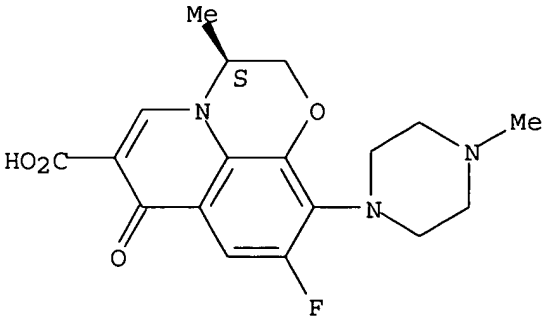
a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

IT **100986-85-4, Levofloxacin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

RN 100986-85-4 CAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:762782 CAPLUS
DOCUMENT NUMBER: 135:322722
TITLE: Coating agents for sustained-release oral preparations containing basic drugs
INVENTOR(S): Nishii, Hiroyuki; Kobayashi, Hirohisa; Otoda, Kazuya
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076557	A1	20011018	WO 2001-JP3024	20010409

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-107671 A 20000410

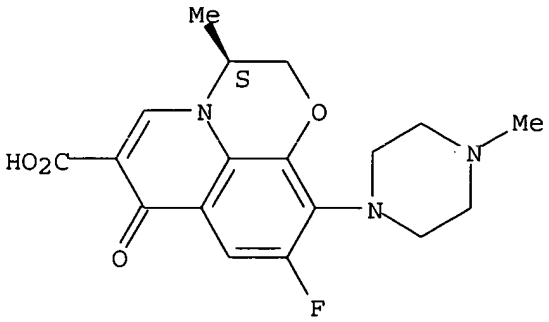
AB Disclosed are pH-independent sustained release prepns. capable of releasing a drug independently from the pH value in the gastric tract. These sustained release prepns. are characterized in that a drug-containing core is coated with (1) a first layer made of a water-insol. polymer, and (2) a second layer made of an enteric polymer and a water-soluble polymer. Core granules were prepared containing perospirone·HCl, **crystalline** cellulose, PVP, starch and silica. The granules were coated with a first composition containing Et cellulose, talc, tri-Et citrate, ethanol, and water, and then a second composition containing methacrylate copolymer, PVP, sucrose ester, Macrogol 6000, and water.

IT **100986-85-4**, **Levofloxacin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymeric coating agents for sustained-release oral prepns. containing basic drugs)

RN 100986-85-4 CAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:114577 CAPLUS

DOCUMENT NUMBER: 132:265211

TITLE: Synthesis and application of levo-ofloxacin analogue

INVENTOR(S): Yang, Yushe; Ji, Ruyun; Chen, Kaixian; Jiang, Huazhen

PATENT ASSIGNEE(S): Shanghai Inst. of Medicines, Chinese Academy of Sciences, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 29 pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

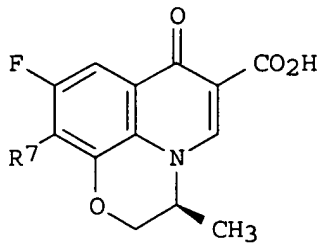
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CN 1181381 A 19980513 CN 1997-106728 19971118
CN 1055927 B 20000830
PRIORITY APPLN. INFO.: CN 1997-106728 19971118
OTHER SOURCE(S): MARPAT 132:265211
GI



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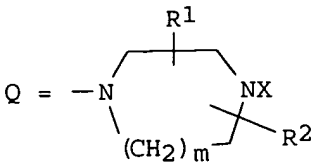
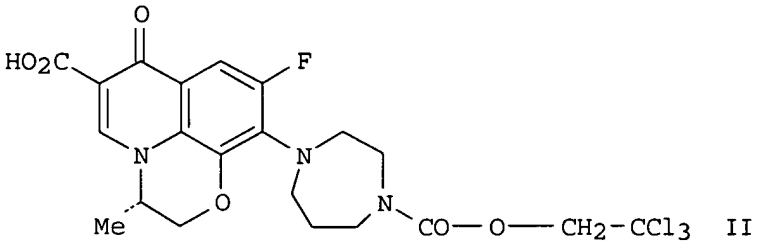




II

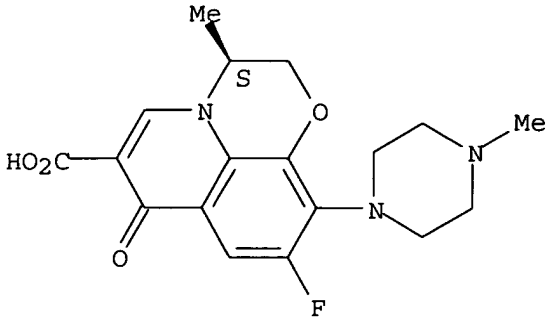
AB Title compds. [I; R7 = Q; X = H, CO2R3, R4, SO2R6; R1 = H, C1-5 alkyl; R2 = H, C1-5 alkyl; R3 = C1-5 alkyl, benzyl; R4 = H, C1-5 alkyl, pyridyl, pyrimidinyl, CO(CH2)nX; X = halo; n = 1, 2; R5 = H, NH2; and R6 = alkyl, substituted phenyl] are prepared as antibacterial, antineoplastic, and anti-mycoplasma agents (no data) by condensation of D-mannitol with acetone and **anhydrous** ZnCl2 as catalyst, oxidin., reduction with KBH4 in methanol to obtain (S)-5,5-dimethyl-1,3-dioxolane-2-methanol, condensation with trifluoro-nitrobenzene in the presence of PTC to obtain (S)-2-(6-nitro-2,3-difluorophenoxy)- 5,5-dimethyl-1,3-dioxolane, hydrolysis to obtain (R)-1-(2,3- dihydroxypropoxy)-6-nitro-2,3-difluorobenzene, bromoacetylation with acetic acid-HBr, cyclization in NaOMe/methanol, redun. with 10% Pd/C as catalyst in **anhydrous** ethanol, substitution with EMME, cyclization with Ph3P in THF, cyclization again with PPE as catalyst, hydrolysis with HCl and acetic acid, and substitution. The title compound II was prepared

IT **100986-85-4P, Levofloxacin 119354-43-7P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and application of levoofloxacin analog)

RN 100986-85-4 CAPLUS

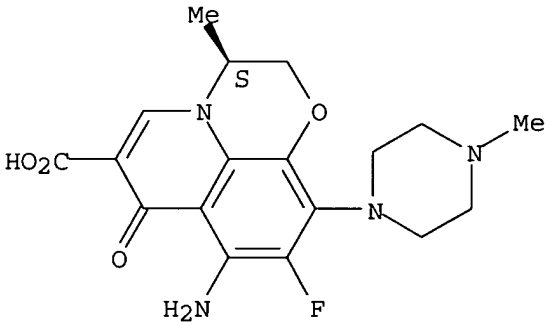
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 119354-43-7 CAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 8-amino-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

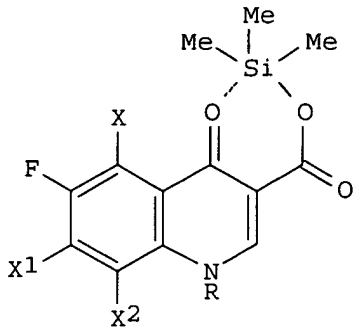


L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:596081 CAPLUS
DOCUMENT NUMBER: 125:247630
TITLE: Trimethylsilyl esters and solvates of chelates of quinoline-3-carboxylic acids, and their preparation and use in a process for quinolone antibacterials.
INVENTOR(S): Palomo Nicolau, Francisco Eugenio; Solis Oller, Jose Maria; Palomo Coll, Antonio Luis
PATENT ASSIGNEE(S): Centro Marga Para La Investigacion S.A., Spain
SOURCE: Span., 14 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2077490	A1	19951116	ES 1992-2560	19921118
ES 2077490	B1	19961016		

PRIORITY APPLN. INFO.: ES 1992-2560 19921118
OTHER SOURCE(S): CASREACT 125:247630; MARPAT 125:247630

GI



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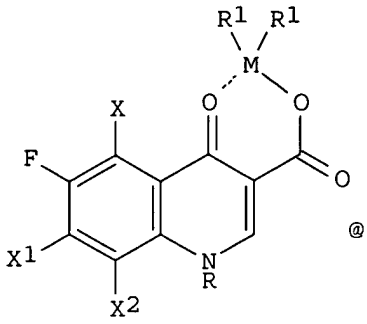
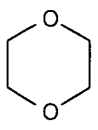
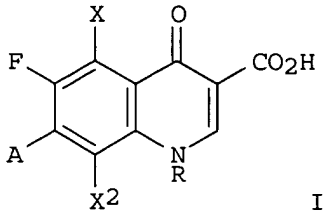




II



III

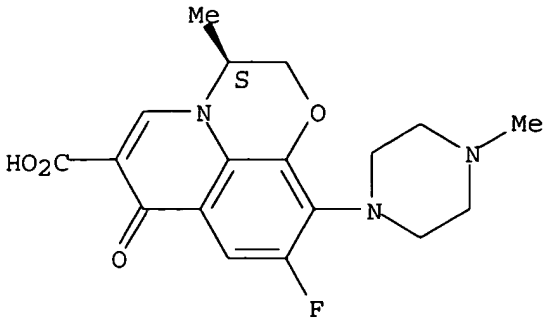
AB Trimethylsilyl esters I and chelates II [X = H, NH2, NHAc, Me; X1 = halo, alkylsulfonyl, arylsulfonyloxy; X2 = H, halo, Me, OMe, OCHF2, OH, SO3H, NO2; when X = H, then X1 and X2 do not both = F; R = alkyl, cycloalkyl, alkylamino, aryl, alkylarom. group; X2R may form 5- or 6-membered heterocycle; M = B, Al; R1 = halo, acyloxy; n = 0.5-2.0] are claimed. The compds. are intermediates for quinolone antibacterials III [A = substituted amino]. For instance, 1-cyclopropyl-7-chloro-1,4-dihydro-6-fluoro-4-oxo-3-quinolinecarboxylic acid reacted with HN(SiMe3)2 in refluxing CHCl3 to give 99% I [X = X2 = H; X1 = Cl; R = cyclopropyl]. This reacted with BF3 in MeCN/1,4-dioxane mixture at 12-15° and then 20-25° to give II [M = B; R1 = F; n unspecified; others as above] in virtually quant. yield. Reaction of this with **anhydrous** piperazine in DMSO at 50-65°, followed by hydrolysis with 10% NaOH at 60°, gave the corresponding III [A = piperazino], i.e. ciprofloxacin.

IT **100986-85-4DP**, boron complexes
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

RN 100986-85-4 CAPLUS

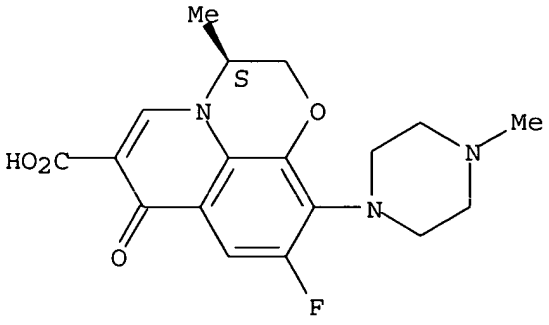
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **100986-85-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)
RN 100986-85-4 CAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



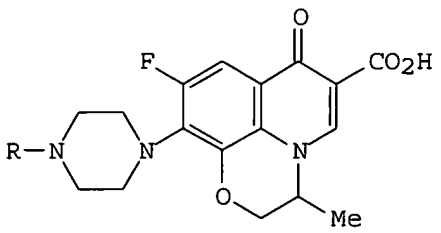
L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:115062 CAPLUS
DOCUMENT NUMBER: 114:115062
TITLE: Antimicrobial pyridobenzoxazines for animals and their preparation
INVENTOR(S): Takahata, Toshihiro; Takei, Masakazu; Kato, Masahiro; Miura, Tadayoshi; Yoshioka, Toshiyuki
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 354453	A2	19900214	EP 1989-114219	19890801
EP 354453	A3	19910410		
EP 354453	B1	19950125		

R: DE, ES, FR, GB, GR, IT, NL					
ES 2070150	T3	19950601	ES 1989-114219		19890801
CA 1339449	A1	19970909	CA 1989-607148		19890801
AU 8939276	A1	19900215	AU 1989-39276		19890803
AU 625066	B2	19920702			
KR 137767	B1	19980515	KR 1989-11102		19890803
JP 02138219	A2	19900528	JP 1989-204197		19890807
JP 2821912	B2	19981105			
CN 1040200	A	19900307	CN 1989-105541		19890809
CN 1042732	B	19990331			
US 5175160	A	19921229	US 1991-747416		19910819
PRIORITY APPLN. INFO.:			JP 1988-198199	A	19880809
			US 1989-391034	B1	19890809

OTHER SOURCE(S): MARPAT 114:115062

GI



I

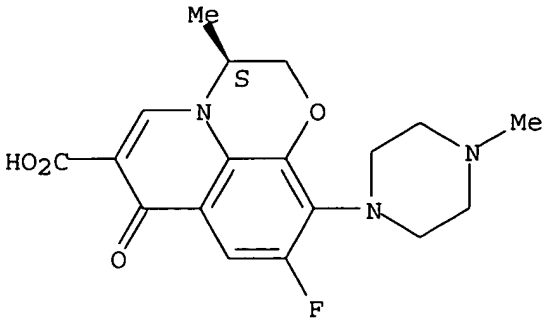
AB 3(RS)- Or 3(S)-pyrido[1,2,3-de][1,4]benzoxazines I (R = C1-6 alkyl) and their salts and hydrates are prepared as veterinary antimicrobials with low toxicity. Thus, 3(RS)-I (R = Bu) (II) was prepared from 3(RS)-I (R = H) and BuBr. II showed a min. inhibitory concentration in vitro of 0.025-0.1 μg/mL against various strains of Mycoplasma gallisepticum. 3(RS)-I (R = Et) was highly effective in vivo at 75 ppm in the feed against M. gallisepticum infections in chickens. An antimicrobial composition for mixing with feed contained active compound 1-10, corn starch 98.5-89.5, and **anhydrous** silicic acid 0.5 weight parts.

IT **100986-85-4**
RL: BIOL (Biological study)
(as veterinary antimicrobial)

RN 100986-85-4 CAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

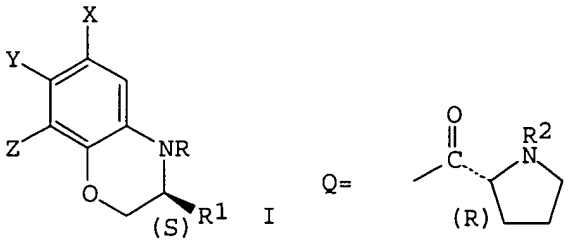
Absolute stereochemistry. Rotation (-).



L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:35875 CAPLUS
DOCUMENT NUMBER: 112:35875
TITLE: Preparation of (S)-3-alkyl-3,4-dihydro-2H-[1,4]benzoxazine derivatives by optical resolution with N-(substituted sulfonyl)-(R)-proline
INVENTOR(S): Fujiwara, Toshihiro; Yokota, Takushi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01175975	A2	19890712	JP 1987-333340	19871229
JP 2724383	B2	19980309		

PRIORITY APPLN. INFO.: JP 1987-333340 19871229
OTHER SOURCE(S): MARPAT 112:35875
GI



AB The title derivs. [(S)-I; R = H; X, Y, Z = H, halo; R1 = C1-6 alkyl], useful as intermediates for antibacterials, e.g. (S)-(-)-9-fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid, are prepared by reaction of (±)-I with an N-(substituted sulfonyl)-(R)-proline and fractional crystallization of the R,S-diastereomer of I (R = Q; R2 = substituted sulfonyl) (II) from the resulting diastereomeric mixts. The process efficiently gives **crystalline** II of high optical purity by recrystn. and is amenable to

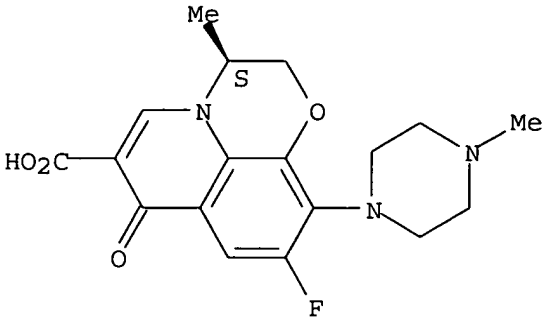
large-scale production of (S)-I. Thus, a solution of (R)-N-(p-toluenesulfonyl)prolyl chloride (prepared from 26.9 g p-MeC6H4SO2-Pr-OH and SOCl2) in ClCH2CH2Cl was added dropwise to a stirred solution of (±)-7,8-difluoro-3-methyl-3,4-dihydro-2H-[1,4]benzoxazine and pyridine in ClCH2CH2Cl to give an oil which was crystallized from EtOAc to give 10:15 g II (R = Q, R1 = Me, X = Z = F, R2 = p-MeC6H4SO2). Treatment of the latter with NaOH in MeOH under reflux gave (S)-(-)-7,8-difluoro-3-methyl-3,4-dihydro-2H-[1,4]benzoxazine of 99% enantiomeric excess.

IT **100986-85-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, difluoromethyldihydrobenzoxazine as)

RN 100986-85-4 CAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

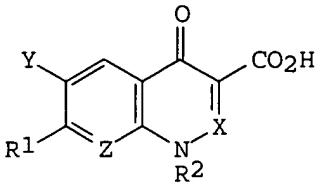
Absolute stereochemistry. Rotation (-).

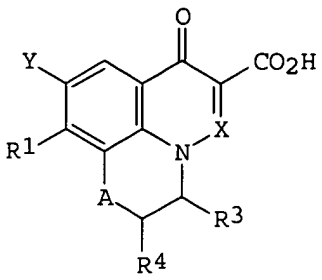


L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:510274 CAPLUS
DOCUMENT NUMBER: 109:110274
TITLE: Preparation of optically active quinolonecarboxylates as antibacterial agents
INVENTOR(S): Duerckheimer, Walter; Leube, Karl
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3639465	A1	19880519	DE 1986-3639465	19861118
EP 268223	A2	19880525	EP 1987-116760	19871113
EP 268223	A3	19900328		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8705055	A	19880519	FI 1987-5055	19871116
AU 8781285	A1	19880519	AU 1987-81285	19871117
AU 602024	B2	19900927		
DK 8706029	A	19880519	DK 1987-6029	19871117
NO 8704786	A	19880519	NO 1987-4786	19871117
JP 63135372	A2	19880607	JP 1987-288602	19871117
ZA 8708593	A	19880629	ZA 1987-8593	19871117

HU 49883 A2 19891128 HU 1987-5098 19871117
HU 199848 B 19900328
PRIORITY APPLN. INFO.: DE 1986-3639465 A 19861118
OTHER SOURCE(S): MARPAT 109:110274
GI


I


II

AB The title compds. [I, II; A = CH2, O, S; R1 = dimethylaminoalkyl, diethylaminoalkyl, heterocyclyl; R2 = (un)substituted alkyl, alkenyl, cyclopropyl; R3, R4 = H, (un)substituted alkyl; X = CH, N, CF; Y = H, halo; Z = alkanoyl] were prepared as antibacterial agents (no data) by N-amination to produce a hydrazinium group, conversion of this product to the zwitterion, resolution via an optically active acid, and cleavage of the salt followed by reductive deamination. (±)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazinyl-6-carboxylic acid (III) was dissolved in H2O with NaHCO3 and aqueous H2NOSO2OH neutralized with NaHCO3 added and the mixture stirred 20 h at room temperature whereupon it was acidified with HCl to give the **crystalline** hydrazinium hydrochloride of III which was converted to the zwitterion with a basic ion exchange resin. The (S)-(+)-mandelic acid salt of the (-)-enantiomer of the latter was crystallized from H2O, treated with ion exchange resin and hydrogenolized to (-)-III.

IT **115972-76-4P 115991-53-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and decomposition of, in resolution of quinolonecarboxylate antibacterials)

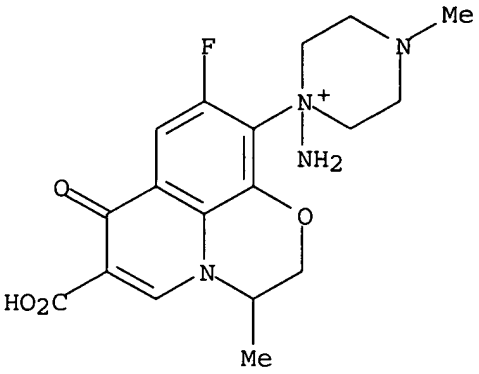
RN 115972-76-4 CAPLUS

CN Piperazinium, 1-amino-1-(6-carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazin-10-yl)-4-methyl-, (-)-, salt with (S)-α-hydroxybenzeneacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 115972-75-3
CMF C18 H22 F N4 O4

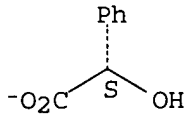
Rotation (-).



CM 2

CRN 4359-03-9
CMF C8 H7 O3

Absolute stereochemistry.

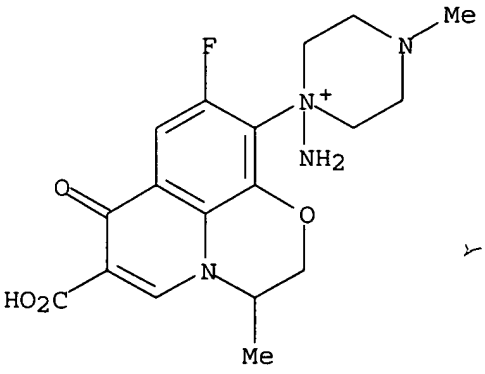


RN 115991-53-2 CAPLUS
CN Piperazinium, 1-amino-1-(6-carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazin-10-yl)-4-methyl-, (+)-, salt with (R)-α-hydroxybenzeneacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 115991-52-1
CMF C18 H22 F N4 O4

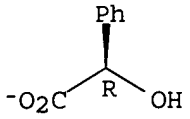
Rotation (+).



CM 2

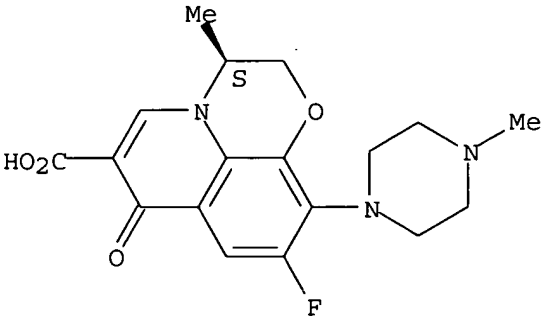
CRN 4359-04-0
CMF C8 H7 O3

Absolute stereochemistry.



IT **100986-85-4P 100986-86-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antibacterial agent)
RN 100986-85-4 CAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 100986-86-5 CAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).